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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,634	01/30/2001	Steven W. Herring	32943/KMO/A97	9937

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/772,634	HERRING ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, IDS AND STATUS OF THE APPLICATION AND CLAIMS

1. The amendment, remarks and Information Disclosure Statement (IDS) and Form PTO-1449 filed 8/15/03 are acknowledged, entered and considered. In view of Applicant's request claims 1-6, 10, 11, 16-21, 23, 24, 28 and 29 have been amended. Thus, claims 1-30 are now pending in the application. With respect to IDS, the references cited therewith are not provided. Hence, the IDS were not considered (See attached Form PTO-1449). The objections to the specification, abstract and claims and the rejections under 35 U.S.C. 112, second paragraph and 35 U.S.C. 103(a) over the prior art of record are withdrawn in view of Applicant's amendment and remarks filed 8/15/03. Applicant's amendment, arguments with respect to the rejection under 35 U.S.C. 103(a) over the prior art of record have been considered but deemed to be moot in view of the new ground of rejection necessitated by Applicant's amendment.

NEW GROUND OF REJECTION

CLAIMS REJECTION-35 U.S.C. § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-12, 14, 15, 19, 20, 22-24 and 26-29 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/39761.

The patent of WO 97/39761 discloses a process for stabilizing lyophilized blood proteins such as Factor VIII (FVIII). The process comprises providing an aqueous solution of a blood protein. Cyclodextrin such as hydroxypropyl-α-cyclodextrin is added to the solution in an amount sufficient to from a stable complex with the protein. The solution is then lyophilized to provide a dry blood protein/cyclodextrin complex. The lyophilized blood protein/cyclodextrin complex is then heated to a temperature and for a time sufficient to inactivate any viral contaminants, preferably to a temperature of at least about 60^0C and more preferably to at least about 80^0C for a time of at least about 10 hours and preferably at least about 72 hours. The viral inactivated blood protein/cyclodextrin complex may be thereafter reconstituted to provide a solution of the blood protein administrable to a patient (See e.g., abstract, summary of the invention and claims 1, 2, and 4-6) as directed to claims 1-5. With respect to the limitation of subjecting the blood protein solution to a solvent detergent viral inactivation step of claim 7, such limitation is clearly disclosed in Examples 1 and 2, which show the use of various solvent detergents for subjecting the blood protein solution in the process of inactivating viral contaminants thereof. On page 3, lines 8-12, the reference clearly states that the cyclodextrin is added in an amount sufficient to assure the formation of a complex with all of the desired blood protein. An amount of cyclodextrin which provides an aqueous solution

having a cyclodextrin concentration of at least about 0.1% preferably from about 0.8% to about 5% weight to volume (wt/vol.) and more preferably about 3% wt/vol. is suitable for most application. Thus, the ranges disclosed overlaps with the ranges of from about 0.5% wt/vol. to about 15% wt/vol. (claim 8); from about 1% wt/vol. to about 12% wt/vol. (claim 9); greater than about 0.1% wt/vol. (claim 10); and from about 1% to about 8% (claim 11), and as such meet the limitations of claims 8-11. (See also claims 3 and 7-8 of WO 97/39761). Further, the reference on page 2, lines 21-26 and on claim 9 discloses a process which incorporates and/or uses blood proteins which are included, but are not limited to albumin, FII, FVII, FVIII, FIX, FX and X_a, fibrinogen, antithrombin III, transferin, haptoglobin, gamma globulins, fibronectin, protein C, protein S, thrombin and C1-inhibitor which meets the limitations of claim 12.

With respect to claims 19 and 20, the claims are in product-by-process format and as such, it is the novelty and patentability of the instantly claimed product that need be established and not the recited process steps, In re Brown, 173 USPQ 685 (CCPA 1972); In re Wertheim, 191 USPQ (CCPA 1976). Further, the prior art described the product as old, In re Best, 195 USPQ 430, 433 (CCPA 1977); (See MPEP 706.03 [e]). Hence, the burden of proving that the process limitation makes a different product is shifted to the Applicants, In re Fitzgerald, 205 USPQ 594.

The prior art as discussed above discloses not only a process, but, also a blood protein product comprising a lyophilized solution of a stable complex

protein and hydroxypropyl-α-cyclodextrin (claim 22), wherein the hydroxypropyl-α-cyclodextrin is present in an amount ranging from about 0.5% wt/vol. to about 15% wt/vol. (claim 23); from about 1% wt/vol. to about 12% wt/vol. (claim 24); or a stabilized blood protein solution comprising a complex of the blood protein and hydroxypropyl-α-cyclodextrin (claim 26), wherein the hydroxypropyl-α-cyclodextrin is present in an amount greater than about 3% wt/vol. (claim 27); from about 0.5% wt/vol. to about 15% wt/vol. (claim 28); and from about 1% wt/vol. to about 12% wt/vol. (claim 29). Thus, in the absence of evidence to the contrary or specific structural limitations, the claimed product disclosed by the reference anticipates product claims 22-24 and 26-29.

It is noted that Applicant has amended the claims from the process of stabilizing.... to a process of enhancing the solubility....,however, as shown above, the prior art clearly discloses that stabilizers such as cyclodextrins including hydroxypropyl-α-cyclodextrin can be used to enhance the solubility of blood protein, and as such anticipates a process for enhancing the solubility of blood protein solution comprising a) adding to a blood protein solution hydroxypropyl-α-cyclodextrin in an amount sufficient to form a stable complex with the protein; and b) lyophilizing the solution of step a) to form a lyophilized complex of the protein and hydroxypropyl-α-cyclodextrin and a blood protein product thereof in the manner claimed in claims 1-5, 7-12, 14, 15, 19, 20, 22-24 and 26-29.

CLAIM REJECTIONS-35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 13, 16-18, 21, 25 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/39761.

The reference WO 97/39761 as discussed in 102(b) rejection above, discloses a process for stabilizing lyophilized blood proteins such as Factor VIII (FVIII). The process comprises providing an aqueous solution of a blood protein. Cyclodextrin such as hydroxypropyl-α-cyclodextrin is added to the solution in an

amount sufficient to from a stable complex with the protein. The solution is then lyophilized to provide a dry blood protein/cyclodextrin complex. The lyophilized blood protein/cyclodextrin complex is then heated to a temperature and for a time sufficient to inactivate any viral contaminants, preferably to a temperature of at least about 60^0C and more preferably to at least about 80^0C for a time of at least about 10 hours and preferably at least about 72 hours. The viral inactivated blood protein/cyclodextrin complex may be thereafter reconstituted to provide a solution of the blood protein administrable to a patient (See e.g., abstract, summary of the invention and claims 1, 2, and 4-6). On page 3, lines 8-12, the reference clearly states that the cyclodextrin is added in an amount sufficient to assure the formation of a complex with all of the desired blood protein. An amount of cyclodextrin which provides an aqueous solution having a cyclodextrin concentration of at least about 0.1% preferably from about 0.8% to about 5% weight to volume (wt/vo.) and more preferably about 3% wt/vol. is suitable for most application. Thus, the ranges disclosed overlaps with the ranges of greater than about 1% wt/vol. (claim 16); and from about 3% wt/vol. to about 8% wt/vol. (claim 17), and as such meet the limitations of claims 16 and 17 (See also claims 3 and 7-8 of WO 97/39761).

The reference differs from claims 6, 13, 16-18, 21, 25 and 30 in not teaching the heating of blood protein solution at temperature of at least 100^0C for at least 1 hour, and the use of blood protein which is fibrinogen and process for enhancing the stability of fibrinogen and product thereof. Although, the preferred

and exemplified blood protein of the reference is FVIII which was stabilized and the solubility of FVIII was enhanced, however, the reference teaches or suggests that other kind of blood proteins can be used and/or incorporated for the same purposes and cites the blood proteins which are included, but are not limited to are albumin, FII, FVII, FVIII, FIX, FX and X_a, fibrinogen, antithrombin III, transferin, haptoglobin, gamma globulins, fibronectin, protein C, protein S, thrombin and C1-inhibitor. Thus, in view of the above, the selection of specific temperature, duration time and the specific blood protein (i.e., fibrinogen), the reference shows the exemplary and preferred blood protein (i.e., FVIII), from the listed blood proteins, ranges for the temperatures, duration time, which overlaps with the claimed ranges and claimed blood proteins. Thus, in view of this, the subject formulation may be used in combination with other condition to provide a wide variety of temperature, duration of time and various blood proteins or may be tailored for specific temperature, duration of time and the type of blood protein (i.e., fibrinogen). Therefore, the claimed specific temperatures, duration of time and the blood protein which is fibrinogen, which fall within the scope of the prior art would have been prima facie obvious from said prior art disclosure to a person of ordinary skill in the art at the time the invention was made. Applicants claims are directed to optimization of an "art recognized variable" which is well within the purview of one of ordinary skill in the art, In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

With respect to claim 21, the claim is in product-by-process format and as such, it is the novelty and patentability of the instantly claimed product that need be established and not the recited process steps, In re Brown, 173 USPQ 685 (CCPA 1972); In re Wertheim, 191 USPQ (CCPA 1976). Further, the prior art described the product as old, In re Best, 195 USPQ 430, 433 (CCPA 1977); (See MPEP 706.03 [e]). Hence, the burden of proving that the process limitation makes a different product is shifted to the Applicants, In re Fitzgerald, 205 USPQ 594.

Thus, the teachings of the prior art makes *prima facie* obvious the claimed invention's process for stabilizing a blood protein solution such as fibrinogen by adding hydroxypropyl-α-cyclodextrin and lyophilizing the solution to from a lyophilized protein/hydroxypropyl-α-cyclodextrin complex or product thereof, absent of sufficient objective factual evidence or unexpected results to the contrary.

CLAIMS REJECTION-35 U.S.C. 112, 2nd PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, lines 4 and 5 are grammatically indefinite in the recitation "any viruses present complex". It appears to be typographical error. Appropriate correction is required.

Claim 6 is inconsistent with claim 5 in the recitation "is heated at least 100^0C". Amendment of the claim to recite "is heated to a temperature of at least 100^0C" is suggested (See e.g., claim 5).

Claim 11 is also inconsistent with other claims in the recitation "from about 1% to about 8%". Amendment of the claim to recite "from about 1% wt/vol. to about 8% wt/vol." is suggested (See e.g., claims 8, 9 and 17).

ACTION IS FINAL, NECESSITATED BY AMENDMENT

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The appropriate fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

/AAM/Mohamed/AAM

October 30, 2003